

WHAT IS CLAIMED IS:

1. A substantially homogenous preparation of N-terminally chemically modified G-CSF or analog thereof,
5 optionally in a pharmaceutically acceptable diluent, carrier or adjuvant.
2. A preparation of claim 1 where said G-CSF is chemically modified with a chemical selected from the
10 group consisting of dextran, poly(n-vinyl pyrrolidone), polyethylene glycols, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols and polyvinyl alcohols.
- 15 3. A preparation of claim 2 where said G-CSF or analog thereof is chemically modified with polyethylene glycol.
- 20 4. A preparation of claim 3 said polyethylene glycol has a molecular weight of between about 2 kDa and 100 kDa.
- 25 5. A preparation of claim 4 wherein said polyethylene glycol has a molecular weight of between about 6 kDa and 25 kDa.
- 30 6. A preparation of claim 1 wherein said preparation is comprised of at least 90% N-terminally monopegylated G-CSF or analog thereof and at most 10% unpegylated G-CSF or analog thereof.

7. A preparation of claim 6 wherein said preparation is comprised of at least 95% N-terminally monopegylated G-CSF or analog thereof and at most 5% unpegylated G-CSF or analog thereof.

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8. A preparation of claim 1 wherein said G-CSF has the sequence identified in SEQ. ID No. 1.

9. A substantially homogenous preparation of
10 N-terminally monopegylated G-CSF, optionally in a pharmaceutically acceptable diluent, carrier or adjuvant, wherein: (a) said G-CSF has the amino acid sequence identified in SEQ. ID No. 1; (b) said G-CSF is
15 monopegylated with a polyethylene glycol moiety having a molecular weight of about 12 kDa.

10. A pharmaceutical composition comprising:
(a) a substantially homogenous preparation of monopegylated G-CSF, said monopegylated G-CSF consisting of a
20 polyethylene glycol moiety having a molecular weight of about 12 kDa connected to a G-CSF moiety solely at the N-terminus thereof via an amine linkage; (b) fewer than 5% non-pegylated G-CSF molecules; and (c) a pharmaceutically acceptable diluent, adjuvant or carrier.

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11. A method of treating a hematopoietic disorder comprising administering a therapeutically effective dose of a preparation of any of claims 1-10.

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✓ 12. A method for attaching a water soluble polymer to a protein or analog thereof, wherein said water

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soluble polymer has a single reactive aldehyde group, said method comprising:

- (a) reacting a protein moiety with a water soluble polymer moiety under reducing alkylation conditions, at a pH sufficiently acidic to selectively activate the α -amino group at the amino terminus of said protein moiety so that said water soluble polymer selectively attaches to said α -amino group; and
- (b) obtaining the reaction product and
- (c) optionally, separating the reaction products from unreacted moieties.

13. A method of claim 12 wherein said polymer is pharmaceutically acceptable.

14. A method of claim 12 wherein said water soluble polymer is selected from the group consisting of dextran, poly(n-vinyl pyrrolidone), polyethylene glycols, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols and polyvinyl alcohols.

15. A method of claim 14 wherein said polymer is polyethylene glycol.

16. A method of claim 12 wherein said reducing alkylation reaction involves the use of a reducing agent selected from sodium borohydride, sodium cyanoborohydride, dimethylamine borate, trimethylamine borate and pyridine borate.

✓ 17. A method for attaching a polyethylene glycol molecule to a G-CSF molecule, wherein said polyethylene glycol molecule has a single reactive aldehyde group, said method comprising:

- 5 (a) reacting said G-CSF with said polyethylene glycol molecule under reducing alkylation conditions, at a pH sufficiently acidic to selectively activate the α -amino group at the amino terminus of said G-CSF; and
- (b) obtaining the pegylated G-CSF and
- 10 (c) optionally, separating the pegylated G-CSF from non-pegylated G-CSF.

18. A method of claim 17 wherein said polyethylene glycol molecule has a molecular weight of
15 about 6 kDa to about 25 kDa.

19. The pegylated G-CSF product produced by the process of claim 17.

20 ~ 20. Chemically modified consensus interferon comprised of a consensus interferon protein moiety connected to at least one water soluble polymer moiety.

21. A chemically modified consensus interferon
25 of claim 20 wherein said consensus interferon moiety is selected from the group consisting of IFN-con₁, IFN-con₂, and IFN-con₃.

22. A chemically modified consensus interferon
30 of claim 21 wherein said water soluble polymer is pharmaceutically acceptable.

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23. A chemically modified consensus interferon of claim 20 wherein said water soluble polymer is selected from the group consisting of dextran, poly(n-vinyl pyrrolidone), polyethylene glycols, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols and polyvinyl alcohols.

24. A chemically modified consensus interferon according to claim 23 wherein said water soluble polymer moiety is polyethylene glycol.

25. A chemically modified consensus interferon according to claim 20 wherein said water soluble polymer moiety is connected to said consensus interferon moiety directly without an additional linkage group.

26. A chemically modified consensus interferon comprised of IFN-con1 connected to at least one polyethylene glycol moiety.

✓ 27. Pegylated consensus interferon.

✓ 28. A method for attaching a water soluble polymer to consensus interferon, wherein said water soluble polymer has a single reactive aldehyde group, said method comprising:

(a) reacting a consensus interferon moiety with a water soluble polymer moiety under reducing alkylation conditions, at a pH sufficiently acidic to selectively activate the α -amino group at the amino terminus of said consensus interferon moiety; and

(b) obtaining the reaction product and

(c) optionally, separating the reaction products from unreacted moieties.

29. A method of claim 28 wherein said polymer
5 is pharmaceutically acceptable.

30. A method of claim 28 wherein said water
soluble polymer is selected from the group consisting of
dextran, poly(n-vinyl pyrrolidone), polyethylene glycols,
10 propylene glycol homopolymers, polypropylene
oxide/ethylene oxide co-polymers, polyoxyethylated polyols
and polyvinyl alcohols.

31. A method of claim 30 wherein said polymer
15 is polyethylene glycol.

32. A method of claim 28 wherein said reducing
alkylation reaction involves the use of a reducing agent
selected from sodium borohydride, sodium cyanoborohydride,
20 dimethylamine borate, trimethylamine borate and pyridine
borate.

✓ 33. A method for attaching a polyethylene
glycol molecule to a consensus interferon molecule, wherein
25 said polyethylene glycol molecule has a single reactive
aldehyde group, said method comprising:

(a) reacting said consensus interferon with
said polyethylene glycol molecule under reducing alkylation
conditions, at a pH sufficiently acidic to selectively
30 activate the α -amino group at the amino terminus of said
consensus interferon; and

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(b) obtaining the pegylated consensus interferon and

(c) optionally, separating the pegylated consensus interferon from non-pegylated consensus
5 interferon.

34. A method of claim 33 wherein said polyethylene glycol molecule has a molecular weight of about 2 kDa to about 100 kDa.

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35. The pegylated consensus interferon product produced by the process of claim 33.

✓ 36. A substantially homogenous preparation of
15 monopegylated consensus interferon.

37. A preparation of claim 36 comprising about 90% monopegylated consensus interferon and about 10% unpegylated consensus interferon.

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✓ 38. A pharmaceutical composition comprising:
(a) a substantially homogenous preparation of monopegylated consensus interferon, said monopegylated consensus interferon consisting of a polyethylene glycol moiety
25 connected to a consensus interferon moiety solely at the N-terminus thereof via an amine linkage; (b) fewer than 5% non-pegylated consensus interferon molecules; and (c) a pharmaceutically acceptable diluent, adjuvant or carrier.

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